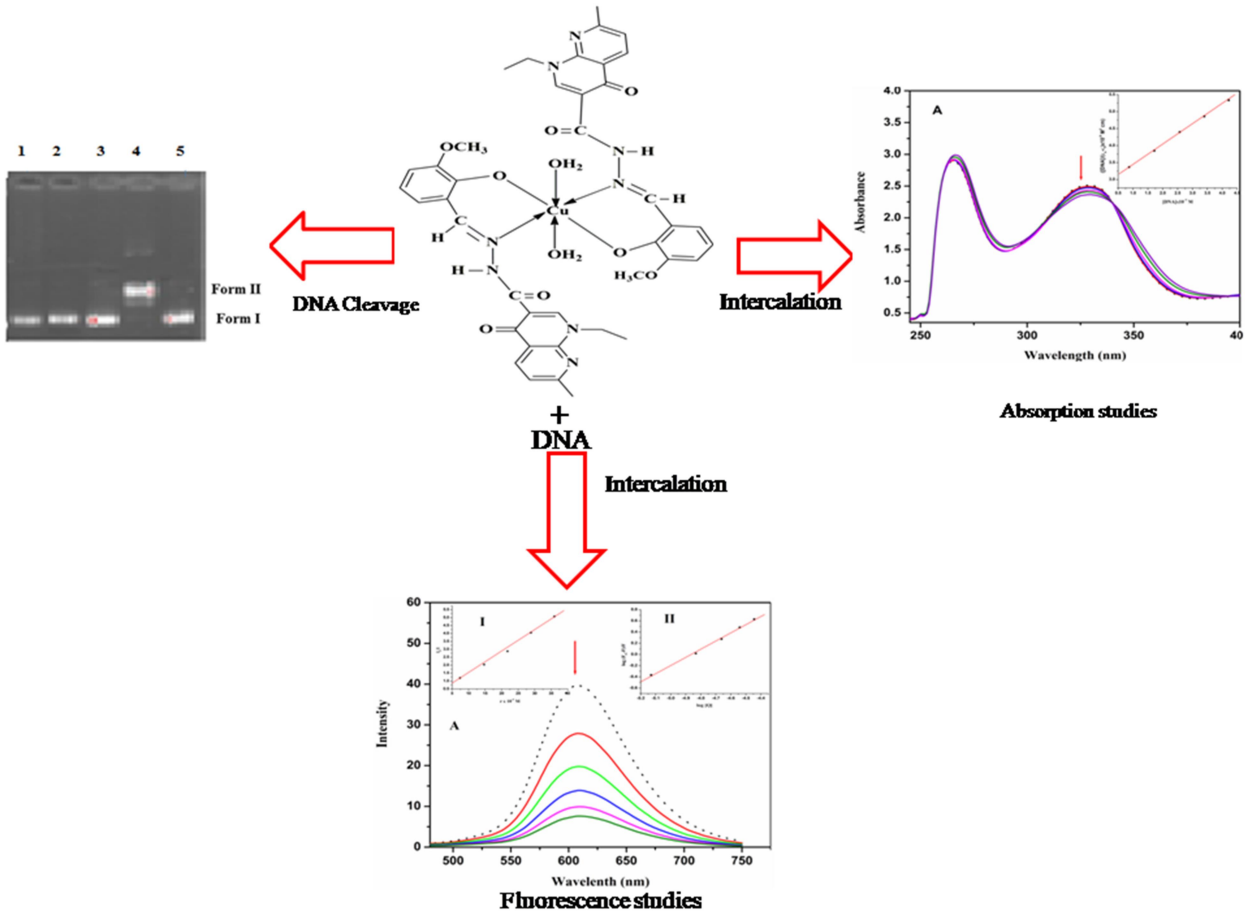
Synthesis, Characterization, DNA Cleavage, Docking and Cytotoxic Studies of Novel Nalidixic acid Hydrazone and its Cu (II), Ni (II) and Co (II) Complexes

Nagula Narsimha[1], Palreddy Ranjithreddy[1], Jaheer Mohmed[1], P Sujitha[1] and Ch. Sarala Devi [1]*

[1*]Department of Chemistry, University College of Science,

Osmania University, Hyderabad -500007, Telangana, India.

*Email ID: dr_saraladevich@yahoo.com



Abstract

Novel N'-(2-hydroxy-3-methoxy-benzylidene)-1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carbohydrazide [NBNCH] and its solid metal complexes with Cu (II), Ni (II) and Co (II) were synthesized and characterized by employing spectro-analytical techniques viz: elemental analyses, Magnetic Susceptibilities Measurements, ^{1}H-NMR, UV-Vis, IR, Mass, TGA, SEM-EDX,

ESR and Spectrophotometry studies. The HyperChem 7.5 software was used for quantum mechanical calculations. The geometry optimization, contour maps of highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) and corresponding binding energy values of molecular and ionic forms of title compound were computed using semi empirical single point PM3 method, in order to understand the binding modes of metal complexes. The stoichiometric studies of complexes determined spectrophotometrically using Job's continuous variation and mole ratio methods inferred 1:2 ratio in respective systems. The title compound and its metal complexes screened for antibacterial and antifungal properties indicated more pronounced activity of Cu (II) complex compared to other compounds. The studies of nuclease activity for the cleavage of PBR322 DNA and MTT assay for in vitro cytotoxic properties showed high activity of Cu (II) complex. The interaction studies of metal complexes with CT-DNA investigated by UV-Visible and fluorescence titrations revealed the intercalation mode of binding. Docking studies were also performed to illustrate the binding mode of the title compound with the target site of "Thymidine phosphorylase from E.coli" (PDB ID: 4EAF) protein.

Key words: Quantum Mechanical Calculations, Antifungal, Docking, DNA Interactions and Cytotoxic Studies